

Amendment filed on February 14, 2001) have been canceled without prejudice to Applicants' right to pursue the subject matter of these canceled claims in related patent applications. In addition, claims 52-59 (corresponding to claims 58-65 as filed in the Preliminary Amendment filed on February 14, 2001) have been amended to correct the claim dependency in view of the misnumbering of claims in the Preliminary Amendment. No new matter has been added. Upon entry of the above-made amendments, claims 51-59 will be pending. A marked version of the amended claims showing changes made is attached hereto as Exhibit A. A clean version of the pending claims, as amended, is attached hereto as Exhibit B.

In the Office Action mailed September 5, 2002, the Examiner has required a restriction to one of the following four groups:

- Group I: Claims 1 and 62-69, drawn to determining the level of one or more disease states in a subject<sup>2</sup>, classified in class 435, subclass 4;
- Group II: Claims 51-59, drawn to diagnosis of a disease, classified in class 435, subclass 4;
- Group III: Claim 60, drawn to determination of the statistical significance of a level of a disease state in an individual, classified in class 435, subclass 4; and
- Group IV: Claim 61, drawn to determination of the statistical significance of a level of the effect of therapy, classified in class 514, subclass 1.

The Examiner contends that the inventions of Groups I-V are distinct, each from the other.

In order to be fully responsive to the Examiner's requirement for a restriction of the instant application, Applicants hereby elect to prosecute Group II, claims 51-59, drawn to diagnosis of a disease, classified in class 435, subclass 4.


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<sup>2</sup> Applicants respectfully point out that claims 62-69 recite a computer system for diagnosing a subject having a disease.

Entry and consideration of the above-made amendments and remarks are respectfully requested.

Respectfully submitted,

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Enclosures

**EXHIBIT A: MARKED VERSION OF AMENDED CLAIMS**  
U.S. APPLICATION SERIAL NO. 09/783,474  
(ATTORNEY DOCKET NO. 9301-123)

(as amended October 4, 2002)

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52. (Amended) The method of claim [57] 51, wherein said interpolated response profile yields a maximum correlation between said diagnostic profile and said interpolated response profile.

53. (Amended) The method of claim [58] 52, wherein said statistical significance of said level of said disease state is determined by comparing the value of said maximum correlation to an expected probability distribution of values of maximum correlation.

54. (Amended) The method of claim [59] 53, wherein said expected probability distribution of values of maximum correlation is obtained by a method comprising

(1) randomizing said diagnostic profile data with respect to cellular constituents to generate a permuted diagnostic profile;

(2) obtaining an interpolated response profile, said interpolated response profile yielding a maximum correlation between said permuted diagnostic profile and said interpolated response profile; and

(3) repeating steps (1) and (2) to construct a probability distribution of values of maximum correlation.

55. (Amended) The method of claim [59] 53, wherein said expected probability distribution of values of maximum correlation is obtained by a method comprising

(1) randomizing said response profile data with respect to the cellular constituents to generate permuted interpolated response curves;

(2) obtaining an interpolated response profile, said interpolated response profile being extracted from said permuted interpolated response curves and yielding a maximum correlation between said diagnostic profile and said interpolated response profile; and

(3) repeating steps (1) and (2) to construct a probability distribution of values of maximum correlation.

56. (Amended) The method of claim [57] 51, wherein said interpolated response profile yields a minimum difference between said diagnostic profile and said interpolated response profile.

57. (Amended) The method of claim [62] 56, wherein said statistical significance of said level of said disease state is determined by comparing the value of the minimum difference to an expected probability distribution of values of minimum difference.

58. (Amended) The method of claim [63] 57, wherein said expected probability distribution of values of minimum difference is obtained by a method comprising

(1) randomizing said diagnostic profile data with respect to the cellular constituents to generate a permuted diagnostic profile;

(2) obtaining an interpolated response profile, said interpolated response profile yielding a minimum difference between said permuted diagnostic profile and said interpolated response profile; and

(3) repeating steps (1) and (2) to construct a probability distribution of values of minimum difference.

59. (Amended) The method of claim [63] 57, wherein said expected probability distribution of values of minimum difference is obtained by a method comprising

(1) randomizing said response profile data with respect to the cellular constituents to generate permuted interpolated response curves;

(2) obtaining an interpolated response profile, said interpolated response profile being extracted from said permuted interpolated response curves and yielding a minimum difference between said diagnostic profile and said interpolated response profile; and

(3) repeating steps (1) and (2) to construct a probability distribution of values of minimum difference.